

REMARKS

Applicants submit this Response to Office Action in response to the Office Action mailed on August 24, 2007 (non-final). Applicants note with appreciation that the Examiner has acknowledged applicants' election without traverse of Group I (claims 1-28) in the reply filed on May 22, 2007; that the Examiner has withdrawn the objection to claim 17; and that the Examiner has withdrawn the 35 USC § 112 rejection of claims 4 and 6. Reconsideration is respectfully requested.

1. Status of the Claims

Claims 1-28 have been rejected. Claim 29 has been withdrawn. Claims 1, 2, 10, 11, 22 and 26 are amended herein, and claims 3, 9, 12 and 13 have been canceled. No new matter is added by these amendments. After entry of the foregoing amendments, claims 1-2, 4-8, 10-11 and 14-28 are pending in this application.

2. Claim Amendments

Applicants have amended independent claim 1 to more clearly recite the subject matter of the presently claimed method for coating ultrafine particles with a polymer. In particular, applicants have amended independent claim 1 to recite that applicants' method includes, *inter alia*, the steps of (i) "suspending a quantity of insoluble ultrafine particles in said solution to form a suspension," (ii) "combining a supercritical fluid as an antisolvent with said suspension in a non-vibrating high pressure vessel to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles," and (iii) wherein the "insoluble ultrafine particles are nanoparticles or submicron particles having a particle size of less than about 500 nm," (iv) wherein the "insoluble ultrafine particles are substantially insoluble in the organic solvent," (v) wherein the "polymer-coated ultrafine particles are in the form of loose agglomerates or individual particles," (vi) wherein the "thickness of the polymer coating on the surface of the polymer-coated ultrafine particles is less than about 75 nm," and (vii) wherein the "antisolvent is combined with the suspension by" (1) "supplying the antisolvent to the non-vibrating high pressure vessel

using the antisolvent supply system;” and (2) “delivering the suspension into the antisolvent using the suspension delivery system.”

Support for the proposed amendments to independent claim 1 is found throughout the specification as filed (see, *e.g.*, paragraphs 25-26, 28, 82-84, 88-89, 93-96, 108-109, 119-120; FIGs. 2 and 4, and the associated text). In view of the foregoing amendments to independent claim 1, applicants have amended dependent claims 2, 10-11, 22 and 26 to conform the dependencies thereof.

As amended, claims 1-2, 4-8, 10-11 and 14-28 are pending in the present application. Applicants respectfully submit that no new matter is introduced by way of the proposed claim amendments, and prompt entry thereof is respectfully requested.

3. Art-Based Rejections

The outstanding Office Action sets forth a rejection under 35 USC § 103(a), as follows:

Claims 1-2, 4-11, 20-22 and 26-28 are rejected under 35 USC § 103(a) as being unpatentable over Subramaniam et al. (USPN 5,833,891) [hereinafter “Subramaniam”]. In addition, claim 19 is rejected under 35 USC § 103(a) as being unpatentable over Subramaniam in view of Lee (USPN 6,596,206) [hereinafter “Lee”].

Applicants respectfully traverse the rejection and submit that the above claims are patentable over Subramaniam and/or Lee, whether taken alone or in combination. Reconsideration of the foregoing Section 103 rejection in view of the claim amendments and remarks set forth herein is respectfully requested.

Applicants respectfully traverse the § 103 rejections based upon Subramaniam and/or Lee, whether taken alone or in combination. Applicants respectfully submit that independent claim 1, as amended, patentably distinguishes over Subramaniam because applicants’ claimed method includes, *inter alia*, the steps of (i) “suspending a quantity of insoluble ultrafine particles in said solution to form a suspension,” (ii) “combining a supercritical fluid as an antisolvent with said suspension in a non-vibrating high pressure vessel to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles,” and (iii) wherein the “insoluble ultrafine particles are nanoparticles or submicron particles having a particle size of less than about 500 nm,” (iv) wherein the

“insoluble ultrafine particles are substantially insoluble in the organic solvent,” (v) wherein the “thickness of the polymer coating on the surface of the polymer-coated ultrafine particles is less than about 75 nm,” and (vi) wherein the “antisolvent is combined with the suspension by” (1) “supplying the antisolvent to the non-vibrating high pressure vessel using the antisolvent supply system;” and (2) “delivering the suspension into the antisolvent using the suspension delivery system.”

Applicants note that Subramaniam fails to teach or suggest a method that includes the noted features and functionalities. Rather, in contrast, Subramaniam teaches two distinctly different processes, wherein the first Subramaniam process taught relates to “small particle precipitation” or “small particle formation” (see, *e.g.*, Subramaniam at col. 1, lines 23-29 and Examples 1-4). As taught in Subramaniam, the small particles that are precipitated or formed are not coated - they are “recovered as particles, or deposited on core particles to form composite particles.” (See Subramaniam at col. 4, line 67 to col. 5, lines 1-2). This first Subramaniam process (*e.g.*, Subramaniam Examples 1-4) is a much different approach and concept compared to the method as recited in applicants’ independent claim 1, as amended, of “combining a supercritical fluid as an antisolvent with said suspension in a non-vibrating high pressure vessel to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles,” wherein the “insoluble ultrafine particles are nanoparticles or submicron particles having a particle size of less than about 500 nm.”

In addition, the second Subramaniam process taught relates to “supercritical fluid coating techniques wherein fluidized core particles are coated with precipitated particles” (see, *e.g.*, Subramaniam at col. 1, lines 33-35 and Examples 5-8). In Subramaniam’s Examples 5-8, core particles (1.5 mm nonpareil sugar beads and 2 mm glass beads) were coated with either a drug or a polymer. This is quite different from applicants’ recited method in independent claim 1, as amended, in several respects. First, applicants’ recited method does not utilize core particles (*e.g.*, Subramaniam uses 1.5 mm nonpareil sugar beads and 2 mm glass beads as the core particles) where “the final coated products can range from micron-sized to several millimeters” (see Subramaniam at col. 7, lines 15-16), and where the “final coatings would typically have a thickness of from about 0.1 μ m to

2mm.” (See Subramaniam at col. 7, lines 17-19). The 1.5 to 2 million nanometer (or 1.5 to 2 mm) core particle size range referred to in the Subramaniam patent (Examples 5-8), are the only examples for coating particles in the Subramaniam patent. The sizes for the core particles in the Subramaniam patent that are coated are substantially greater than the polymer-coated “nanoparticles or submicron particles having a particle size of less than about 500 nm” as claimed in applicants’ claim 1, as amended. In other words, the size of the coated core particles resulting from the Subramaniam method are substantially larger than the coated “nanoparticles or submicron particles having a particle size of less than 500 nm” as claimed in applicants’ method. Indeed, Subramaniam and/or Lee lacks any teaching, suggestion and/or disclosure of a method having polymer-coated ultrafine particles wherein the ultrafine particles are “nanoparticles or submicron particles having a particle size of less than about 500 nm” as claimed in applicants’ coating method, as amended. In addition, applicants’ claimed method, as amended, provides that “the thickness of the polymer coating on the surface of the polymer-coated ultrafine particles is less than about 75 nm.” In contrast, Subramaniam’s method requires that the “final coatings . . . have a thickness of from about 0.1 μ m to 2mm [100 nm to 2 million nanometers].” (See Subramaniam at col. 7, lines 17-19).

Furthermore, the Subramaniam patent does not disclose or suggest the coating method as claimed by applicants “wherein the polymer concentration of said polymer with respect to said solvent in said solution is less than about 4.0 mg/ml so as to minimize agglomeration of said polymer-coated ultrafine particles.” (See Subramaniam patent, Examples 5-8, which are the only examples for coating particles in the Subramaniam patent). In addition, unlike Subramaniam, applicants’ claimed method, as amended, does not utilize core particles in a fluidized gas stream to effect the coating. In Subramaniam, the particles to be coated are first charged into a vessel, along with the antisolvent (CO_2), and then the solution (which includes the coating agent, but does not include the particles to be coated) is pumped into the vessel. (See, e.g., Subramaniam patent, Example 5). In sharp contrast, applicants’ claimed method provides that the insoluble ultrafine particles to be coated are suspended in a solution of a polymer (coating polymer) in an organic solvent to form a suspension, and that the suspension (which includes the coating polymer and the insoluble ultrafine particles to be coated) is then delivered into the antisolvent contained in

a vessel. In other words, Subramaniam teaches that the particles to be coated are already in a vessel along with the antisolvent, and then the polymer solution (**not** containing the particles to be coated) is then pumped into the vessel. In contrast, applicants' claimed method recites that the insoluble particles to be coated are suspended in the polymer solution to form a suspension, and then the suspension (containing the particles to be coated) is delivered into the antisolvent contained in the vessel. Indeed, Subramaniam and/or Lee lacks any teaching, suggestion and/or disclosure of a method that includes, *inter alia*, the steps of (i) "preparing a solution of a polymer in an organic solvent," (ii) "suspending a quantity of insoluble ultrafine particles in said solution to form a suspension," and (iii) "delivering the suspension into the antisolvent using the suspension delivery system."

For at least the foregoing reasons, applicants respectfully submit that independent claim 1, as amended, patentably distinguishes over Subramaniam. In addition, applicants respectfully submit that dependent claims 2, 4-8, 10-11, 14-28, which depend directly or indirectly from independent claim 1, patentably distinguish over Subramaniam and/or Lee, whether taken alone or in combination, for at least the reasons noted with respect to independent claim 1.

Claims 1, 5-8, 10-11, 14-18 and 26 are rejected under 35 USC § 103(a) as being unpatentable over Gupta et al. (USPN 6,620,351), [hereinafter "Gupta"]. Applicants respectfully traverse the rejection and submit that the above claims are patentable over Gupta. Reconsideration of the foregoing Section 103 rejection in view of the claim amendments and remarks set forth herein is respectfully requested.

Applicants respectfully traverse the § 103 rejections based upon Gupta. Applicants respectfully submit that independent claim 1, as amended, patentably distinguishes over Gupta because applicants' claimed method includes, *inter alia*, the steps of (i) "suspending a quantity of insoluble ultrafine particles in said solution to form a suspension," (ii) "combining a supercritical fluid as an antisolvent with said suspension **in a non-vibrating high pressure vessel** to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles," and (iii) wherein the "insoluble ultrafine particles are

nanoparticles or submicron particles having a particle size of less than about 500 nm,” (iv) “wherein the polymer concentration of said polymer with respect to said solvent in said solution is less than about 4.0 mg/ml so as to minimize agglomeration of said polymer-coated ultrafine particles,” (v) wherein the “polymer-coated ultrafine particles are in the form of loose agglomerates or individual particles,” (vi) wherein the “thickness of the polymer coating on the surface of the polymer-coated ultrafine particles is less than about 75 nm,” and (vii) wherein the “antisolvent is combined with the suspension by supplying the antisolvent to the **non-vibrating high pressure vessel** using the antisolvent supply system.”

Applicants respectfully traverse the rejection and submit that the above claims are patentable over Gupta. Reconsideration of the foregoing Section 103 rejection in view of the claim amendments and remarks set forth herein is respectfully requested.

Applicants note that Gupta fails to teach or suggest a method that includes the noted features and functionalities. Rather, in contrast, Gupta teaches a method for making encapsulated core particles (*e.g.*, magnetite) with a desired substance to form composite nanoparticles by combining **on a vibrating surface** an antisolvent at or near supercritical conditions with a dispersion of the substance having core particles held in suspension in the dispersion. The Gupta approach is a much different approach and concept compared to the method as recited in applicants’ independent claim 1, as amended. The Gupta method teaches that it is critical to utilize a “**vibrating surface** (*e.g.*, Gupta’s ‘horn surface 13’) that atomizes the jet into micro-droplets,” and that “change in vibration intensity is used to decrease the particle size of such coated or encapsulated particles.” (See Gupta at col. 4, lines 66-67; col. 6, lines 42-43). The Gupta approach is a much different approach and method compared to the method as recited in applicants’ independent claim 1, as amended, of “combining a supercritical fluid as an antisolvent with said suspension **in a non-vibrating high pressure vessel** to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles,” wherein the “insoluble ultrafine particles are nanoparticles or submicron particles having a particle size of less than about 500 nm.”

Furthermore, the Gupta patent does not disclose or suggest the coating method as claimed by applicants “wherein the polymer concentration of said polymer with respect to

said solvent in said solution is less than about 4.0 mg/ml so as to minimize agglomeration of said polymer-coated ultrafine particles,” and “wherein the polymer-coated ultrafine particles are in the form of loose agglomerates or individual particles.” (See Gupta patent, Example 5, which is the only example for coating particles in the Gupta patent).

In contrast, the Gupta patent (Gupta, Example 5) teaches a method for making encapsulated core particles “to form composite nanoparticles,” wherein the core particles are “encapsulated in the polymer matrix.” (See Gupta, col. 14, lines 60-62; col. 15, lines 11-13). In other words, Gupta teaches a method for producing a large composite aggregate (e.g., a matrix of particles surrounded by polymer) of at least 10 times the single particle size. (See Gupta, Example 5). With the Gupta coating method, the final product is a large polymer chunk with particles embedded within. Applicants’ claimed method, on the other hand, provides for the coating of individual nano or submicron particles with polymer in a core/shell structure (e.g., particle/polymer structure), rather than producing a large composite aggregate (e.g., a matrix of particles surrounded by polymer) as taught in Gupta. In addition, and in further contrast to the Gupta method, applicants’ claimed method recites that “the polymer concentration” in the solvent must be “less than about 4.0 mg/ml so as to minimize agglomeration” of the individual core/shell coated particles, in order to prevent production of a large matrix-like structure or large composite, as taught by Gupta. The Gupta method also teaches utilizing a polymer content that is at least twice as great as compared to the polymer content in applicants’ claimed method, further highlighting the fact that the Gupta method teaches the production of a large matrix-like structure (e.g., a matrix of particles surrounded by polymer), rather than the coating of individual particles with polymer in a core/shell structure as in applicants’ claimed method.

Indeed, Gupta lacks any teaching, suggestion and/or disclosure of a method that includes, *inter alia*, the steps of (i) “suspending a quantity of insoluble ultrafine particles in said solution to form a suspension,” (ii) “combining a supercritical fluid as an antisolvent with said suspension in a non-vibrating high pressure vessel to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles,” and (iii) wherein the “insoluble ultrafine particles are nanoparticles or submicron particles having a particle size of less than about 500 nm,” (iv) wherein the “polymer-coated ultrafine

particles are in the form of loose agglomerates or individual particles,” (v) wherein the “thickness of the polymer coating on the surface of the polymer-coated ultrafine particles is less than about 75 nm,” and (vi) wherein the “antisolvent is combined with the suspension by supplying the antisolvent to the non-vibrating high pressure vessel using the antisolvent supply system.”

For at least the foregoing reasons, applicants respectfully submit that independent claim 1, as amended, patentably distinguishes over Gupta. In addition, applicants respectfully submit that dependent claims 5-8, 10-11, 14-18 and 26, which depend directly or indirectly from independent claim 1, patentably distinguish over Gupta for at least the reasons noted with respect to independent claim 1.

Claims 1, 2, 11, 18 and 22 are rejected under 35 USC § 103(a) as being unpatentable over Perrut (U.S. Pub. No. 2003/0031784), [hereinafter “Perrut”]. In addition, claims 23-25 are rejected under 35 USC § 103(a) as being unpatentable over Perrut in view of Lee (USPN 6,596,206) [hereinafter “Lee”].

Applicants respectfully traverse the rejection and submit that the above claims are patentable over Perrut and/or Lee, whether taken alone or in combination. Reconsideration of the foregoing Section 103 rejection in view of the claim amendments and remarks set forth herein is respectfully requested.

Applicants respectfully traverse the § 103 rejections based upon Perrut and/or Lee, whether taken alone or in combination. Applicants respectfully submit that independent claim 1, as amended, patentably distinguishes over Perrut because applicants’ claimed method includes, *inter alia*, the steps of (i) “suspending a quantity of insoluble ultrafine particles in said solution to form a suspension,” (ii) “combining a supercritical fluid as an antisolvent with said suspension in a non-vibrating high pressure vessel to cause the polymer to precipitate from said solution and coat the surface of at least a portion of said quantity of suspended ultrafine particles to produce polymer-coated ultrafine particles,” and (iii) wherein the “insoluble ultrafine particles are nanoparticles or submicron particles having a particle size of less than about 500 nm,” (iv) wherein the “insoluble ultrafine particles are substantially insoluble in the organic solvent,” (v) wherein the “thickness of the polymer coating on the surface of the polymer-coated ultrafine particles is less than

about 75 nm,” and (vi) wherein the “antisolvent is combined with the suspension by” (1) “supplying the antisolvent to the non-vibrating high pressure vessel using the antisolvent supply system;” and (2) “delivering the suspension into the antisolvent using the suspension delivery system.”

Applicants note that Perrut fails to teach or suggest a method that includes the noted features and functionalities. Rather, in contrast, Perrut teaches a method of where the particles to be coated are dispersed in a fluid at supercritical pressure (the antisolvent), wherein the **particles to be coated** (e.g., amoxicillin) are contained in the antisolvent (carbon dioxide gas), and then a solution containing ethylcellulose as the coating agent (but not containing the particles to be coated) in ethyl acetate is contacted with the antisolvent containing the particles to be coated. (See Perrut at Example 1, para. 54). In Perrut, the particles to be coated (e.g., amoxicillin) are contained/dispersed within the antisolvent, and then the antisolvent containing the particles to be coated is percolated within the ethyl acetate solution containing ethylcellulose (e.g., coating polymer) to obtain the microcapsule particles of amoxicillin. (See Perrut at Example 1, para. 54). In contrast, applicants’ claimed method provides that the particles to be coated (e.g., the ultrafine particles) are suspended in the solution containing the polymer (e.g., coating polymer) prior to combining the suspension with the antisolvent. In other words, applicants’ claimed method provides that the insoluble ultrafine particles to be coated are suspended in a solution of a polymer in an organic solvent to form a suspension, and that the suspension (which includes the coating polymer **and** the insoluble ultrafine particles to be coated) is then delivered into the antisolvent contained in a vessel. Perrut, on the other hand, teaches that the particles to be coated are already contained/dispersed within the antisolvent, and then the polymer solution (not containing the particles to be coated) is then contacted with the particle-laden antisolvent. Indeed, Perrut and/or Lee lacks any teaching, suggestion and/or disclosure of a method that includes, *inter alia*, the steps of (i) “preparing a solution of a polymer in an organic solvent,” (ii) “suspending a quantity of insoluble ultrafine particles in said solution to form a suspension,” and (iii) “delivering the suspension into the antisolvent using the suspension delivery system.” Furthermore, Perrut does not disclose or suggest the coating method as claimed by applicants “wherein the polymer


concentration of said polymer with respect to said solvent in said solution is less than about 4.0 mg/ml so as to minimize agglomeration of said polymer-coated ultrafine particles.”

For at least the foregoing reasons, applicants respectfully submit that independent claim 1, as amended, patentably distinguishes over Perrut. In addition, applicants respectfully submit that dependent claims 2, 11, 18, 22 and 23-25, which depend directly or indirectly from independent claim 1, patentably distinguish over Perrut and/or Lee for at least the reasons noted with respect to independent claim 1.

Accordingly, for at least the stated reasons, claims 1-2, 4-8, 10-11 and 14-28 are believed to be neither taught nor suggested by Subramaniam, Gupta, Perrut and/or Lee and, therefore, are neither anticipated by, nor rendered obvious in view of, Subramaniam, Gupta, Perrut and/or Lee, whether taken alone or in combination with one another, or in combination with the other art of record. Reconsideration and prompt allowance of all pending claims are respectfully requested. If the examiner believes that a telephone conversation may be useful in advancing prosecution of the application, the examiner is invited to contact applicants' undersigned counsel.

Respectfully submitted,

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